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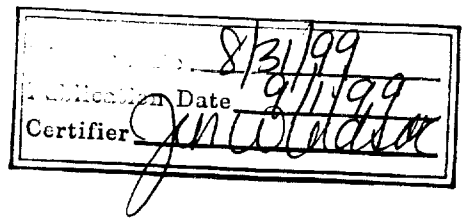

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99D–2445]

Draft Guidance for Industry on Clinical Considerations for Accelerated and Traditional Approval of Antiretroviral Drugs Using Plasma HIV RNA Measurements; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Clinical Considerations for Accelerated and Traditional Approval of Antiretroviral Drugs Using Plasma HIV RNA Measurements.'' The draft guidance is intended to assist pharmaceutical sponsors in the development of antiretroviral drugs and to serve as a focus for continued discussion among the agency, the public, industry, and scientific communities regarding the use of plasma human immunodeficiency virus (HIV) ribonucleic acid (RNA) measurements in phase 3 clinical studies of antiretroviral drugs.

DATES: Written comments on the draft guidance may be submitted by (*insert date 90 days after date of publication in the* **Federal Register**). General comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of the draft guidance for industry are available on the Internet at ''http://www.fda.gov/cder/guidance/index.htm''. Submit written requests for single copies of the draft guidance entitled ''Clinical Considerations for Accelerated and Traditional Approval of Antiretroviral Drugs Using Plasma HIV RNA Measurements'' to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in

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processing your requests. Submit written comments concerning the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5600 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Jeffrey S. Murray, Center for Drug Evaluation and Research (HFD–530), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2495.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance for industry entitled ''Clinical Considerations for Accelerated and Traditional Approval of Antiretroviral Drugs Using Plasma HIV RNA Measurements.'' The draft guidance summarizes the scientific basis supporting the use of HIV RNA as a primary study endpoint in both accelerated and traditional approvals of antiretroviral drugs. This summary is based on scientific data presented at a July 14 and 15, 1997, meeting of the Antiviral Drugs Advisory Committee. At this meeting, there was expert consensus that the use of plasma HIV RNA endpoints in certain situations could reliably predict clinical benefit. The draft guidance suggests that accelerated approvals could be based on studies that show a drug's contribution toward shorter-term reductions in HIV RNA (e.g., 24 weeks) while traditional approvals could be based on trials that show a drug's contribution toward durability of HIV RNA suppression (e.g., at least 48 weeks) in lieu of a traditional clinical endpoint study. Changes in CD4 cell counts should be consistent with observed HIV RNA changes when considering approval of an antiretroviral drug.

The draft guidance describes the agency's current thinking on clinical trial designs using HIV RNA changes as an endpoint for accelerated and traditional approvals. Considerations regarding control arms, study procedures, endpoints, and statistical methods for analyzing HIV RNA endpoints are discussed. The draft guidance also includes recommendations for sponsors who plan to use a new or unapproved HIV RNA assay in a clinical study. When using such assays, sponsors are encouraged to provide supporting data on the assay's limits and performance characteristics as outlined in the last section of the draft guidance.

This Level 1 draft guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on certain aspects of antiretroviral drug product development for accelerated and traditional approval. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Interested persons may, at any time, submit written comments on the draft guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number

found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: 8/20/99
August 20, 1999

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

Margaret M. Dotzel
Acting Associate Commissioner for Policy

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